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09/771,382	01/25/2001	Ian Richard Anselm Peak	8795-24 U1	6450

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FORD, VANESSA L

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Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No. 09/771,382	Applicant(s) PEAK ET AL.	
	Examiner Vanessa L. Ford	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-32* is/are pending in the application.

4a) Of the above claim(s) *26,27 and 29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24,25,28 and 30-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11&14* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence alignments* .

DETAILED ACTION

1. Applicant's election without traverse of Group II, claims 10-16, SEQ ID No: 11, residues 109-120 filed on April 22, 2002 is acknowledged. Claims 1-23 have been cancelled. Claims 24-32 have been added. Claims 24, 25, 28 and 30-32 will be examined in respected to the elected invention, SEQ ID NO: 11. Claims 26-27 and 29 will not be examined because they are drawn to non-elected species. The requirement to elected specific residues (i.e. residues 109-120) is withdrawn.

The traversal is on the grounds that the election of species and the required elected amino acid residues are not independent and distinct, therefore the examination of the entire application does not constitute a serious burden. These arguments have been fully considered but are not found to be persuasive for the reasons below:

First, the classification system has no statutory recognition whether inventions are independent and distinct. For example, each class and subclass is comprised of numerous completely independent and distinct patented inventions.

Second, MPEP 803 states that restriction is proper between patentably distinct inventions where the inventions are (1) independent or distinct as claimed and (2) a serious search and examination burden is placed on the examiner if restriction is not required.

The term "distinct" is defined to mean that two or more subjects as disclosed are related, for example as product and method of use, etc., but are capable of separate manufacture, use or sale as claimed, and are patentable over each (see MPEP 802.01). In the instant situation, the inventions of Groups I-V are drawn to distinct inventions

which are separate products and methods capable of separate manufacture, use or sale as described in the previous Office Action.

Classification of the subject matter is merely one indication of the burdensome nature of the search. The literature search, particularly relevant in this art, is not co-extensive, because for example, Groups I, III and IV are drawn to different products. Groups II and V are drawn to different methods which require different method steps, parameters and endpoints. Clearly different searches and issues are involved in the examination of each Group. Although SEQ ID NO: 11 is a consensus of SEQ ID NOs: 1-10, it must be remembered that each of the sequences (i.e. SEQ ID No. 1-11) are structurally different.

For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Specification Objections

2. The specification is objected because of the use of worldwide web addresses on page 49, line 25. The worldwide web address can be readily changed and therefore, may not be available to the public. The specification should be reviewed for worldwide web addresses and the web address must be deleted from the specification.

3. The specification is objected to because of the following informalities: Page 3, line 29 states Figure 14, there is not Figure 14, the Figures are labeled Figure 14A-14G. Correction is required.

Drawings

4. The drawings are objected to by the Draftsman under 37 CFR 1.84 or 1.152. See the attached form PTO 948.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 24-28, 28 and 30-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. *This is a written description rejection.*

The specification broadly describes as a part of the invention polypeptides that are variants or fragments of SEQ ID No. 11. The specification discloses the claimed invention also contemplates fragments, derivatives and variants (such as allelic variants) of the exemplified proteins (page 13). The specification states " that amino acids can be deleted from any of the C1-5 sequences set forth in Figure 1, while not all non-conserved amino acids in the V1-4 regions need be deleted in order to reduce strain-specific immunogenicity and isolated proteins of the invention may include fragments of the C1-5 and V1-4 regions" (page 13). The specification also states " that a "fragment" includes an amino acid sequence that constitutes less than 100%, but at

least 20%, preferably 50%, more preferably at least 80% or even more preferably at least 90% of said C1, C2, C3 C4 or C5 regions". Applicant has broadly described the invention as embracing any substitution, insertion or deletion change of amino acids throughout the length of the polypeptide sequence. Variants or fragments of SEQ ID No: 11 correspond to sequences from other species, mutated sequences, allelic variants, splice variants, sequences that have a variant degree of identity (similarity, homology), and so forth. None of these sequences meet the written description provision of 35 U.S.C. 112, first, paragraph. The specification provides insufficient written description to support the genus encompassed by the claim. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of allelic variants or fragments of SEQ ID NO: 11 that are encompassed by the polypeptides of the invention regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to

mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Therefore, the full breadth of the claim (or none of the sequences encompassed by the claim, i.e. variants or fragments of SEQ ID No: 11) does not meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

7. Claims 31-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not enable how to use the claimed vaccine for protection. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims 31-32 are drawn to isolated protein comprising at least twelve contiguous amino acid of a conserved region of SEQ ID No:11, wherein a the isolated protein is not a wild-type NhhA polypeptide and wherein the protein is capable of eliciting an immune response against one or strains of *N. meningitidis* and a vaccine comprising the protein.

The specification fails to teach how to use the claimed vaccines for protection. The term "vaccine" encompasses the ability of the specific antigen to induce protective immunity to a bacterial infection or disease induction. The specification discloses that the claimed compositions may be used as therapeutic or prophylactic vaccines and that

the production of vaccines containing as actives one or more immunogenic agents of the invention (page 34). The specification teaches that mice were inoculated with purified wild-type NhhA polypeptides and detection mutants, blood was taken and serum extracted. The specification teaches that the sera was tested for the presence of antibodies recognizing the full length NhhA by Western immunoblot. The specification further states " that it is possible to elicit an immune response against the full length mature NhhA polypeptide by inoculation with deletion mutants or with the full length mature NhhA polypeptides" (page 53 and Figure 13). The specification does not provide substantive evidence that the claimed vaccines are capable of inducing protective immunity. This demonstration is required for the skilled artisan to be able to use the claimed vaccines for their intended purpose of treating bacterial infections. Without this demonstration, the skilled artisan would not be able to reasonably predict the outcome of the administration of the claimed vaccines, i.e. would not be able to accurately predict if protective immunity has been induced. The ability to reasonably predict the capacity of a single bacterial immunogen or combinations of immunogens to induce protective immunity from *in vitro* antibody reactivity studies is problematic. Ellis *(Vaccines, W.B. Saunders Company, 1988, Chapter 29)* exemplifies this problem in the recitation that "the key to the problem (of vaccine development) is the identification of a protein component of a virus or microbial pathogen that itself can elicit the production of protective antibodies"(page 572, second full paragraph). Unfortunately, the art is replete with instances where even well characterized antigens that induce an *in vitro* neutralizing antibody response fail to elicit *in vivo* protective immunity. Boslego et al

(*Vaccines and Immunotherapy, Pergaman Press, 1991, Chapter 17)* teach a single gonococcal pillin protein wherein the protein fails to elicit protective immunity even though a high level of serum antibody response is induced (page 212, bottom of column 2). Accordingly, the art indicates that it would require undue experimentation to formulate and use a successful vaccine without the prior demonstration of vaccine efficacy.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to developing a vaccine that would achieve a desire level of success when administered to a patient with a bacterial infection that is capable of treating that bacterial infection, 3) there are limited working examples which suggest the desired results of a vaccine against *Neisseria meningitidis* 4) the nature of the invention involved the complex and incompletely understood area of protective immune responses against *Neisseria meningitidis* , 5) the relative skill of those in the art is commonly recognized as quite high (post - doctoral level), and the

lack of predictability in the field to which the invention pertains is recognized in the art as evidenced by the cited prior art.

In view of all of the above, in view of the lack of predictability in the art, it is determined that it would require undue experimentation to make and use the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 24 recite the term "capable of ". It is unclear as to what the applicant is referring? Thus, the metes and bounds of "capable of " cannot be ascertained. Clarification as to the meaning of this term is required.

9. Claim 31 is rejected under 35 USC 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The language of the claims is not as precise as the subject matter permits such that one may reasonably know the metes and bounds of the claims. Claim 31 is drawn to a pharmaceutical composition which only contains proteins. It is unclear as to what Applicant intends by "composition" because no pharmaceutical carrier is contained in the composition. Clarification is requested in order to overcome this rejection.

Claim R jections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

10. Claims 24-25 and 31-32 are rejected under 35 U.S.C. 102(e) as anticipated by Peak et al *(U.S. Patent No. 6,197, 312, published March 6, 2001).*

Claims 24-25 and 31-32 are drawn to an isolated protein comprising at least twelve contiguous amino acids of a conserved region of SEQ ID NO:11, wherein the isolated protein is not a wild-type NhhA polypeptide and wherein the protein is capable of eliciting an immune response against one or more strain of *N. meningitidis*.

Peak et al teach an isolated polypeptide from *Neisseria meningitidis* and pharmaceutical compositions containing the polypeptide (see the Abstract). Peak et al teach pharmaceutical compositions for treating patients against *N. meningitidis* infections which comprises polypeptides, fragments, variants or derivatives and a pharmaceutically acceptable carrier (column 16, lines 6-64). Peak et al teach that the compositions of the invention may be used as therapeutic or prophylactic vaccines (column 16, lines 65-66). The claimed isolated protein comprising at least twelve

contiguous amino acids of a conserved region of SEQ ID NO: 11 (i.e. amino acid residues 109-120) is the same as amino acid residues 105-116 of SEQ ID NO: 5 of the prior art (see attached sequence alignment). The protein, pharmaceutical composition and vaccine of Peak et al appears to be the same as the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's protein, pharmaceutical composition and vaccine with the protein, pharmaceutical composition and vaccine of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein, pharmaceutical composition and vaccine of the prior art does not possess the same material structural and functional characteristics of the claimed protein, pharmaceutical composition and vaccine). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

11. Claim 30 is rejected under 35 U.S.C. 102(b) as anticipated by *Zhao et al (Mol Gen Genet, August 1990, 223(1):163-166).*

Claim 30 is drawn to an allelic variant of the isolated protein of claims 24.

Zhao et al teach a protein from *Xanthomonas campestris pv. translucens* that is an allelic variant of SEQ ID NO: 11. The protein of the prior art has 19.2% similarity to the SEQ ID NO:11 *(see attached sequence alignment).*

Given that the claim does not recite any level of sequence identity required to be an allelic variant, the molecule disclosed by Zhao et al is deemed to be an allelic variant.

12. Claim 30 is rejected under 35 U.S.C. 102(b) as anticipated by Gilmore et al *(Mol Microbiology, November 1989, 3(11):1579-1586).*

Claim 30 is drawn to an allelic variant of the isolated protein of claims 24.

Gilmore et al teach a 120 kD protein from Rickettsia rickettsii that is an allelic variant of SEQ ID NO: 11. The protein of the prior art has 21.4% similarity to the SEQ ID NO:11 *(see attached sequence alignment).*

Given that the claim does not recite any level of sequence identity required to be an allelic variant, the molecule disclosed by Gilmore et al is deemed to be an allelic variant.

Pertinent Prior Art

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure *(Peak et al, WO 99311132, published June 1999 and Grandi et al, WO 9936544, published July 1999).*

Status of Claims

14. No claims are allowed.

Conclusion

15. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
July 10, 2002

MARK NAVARRO
PRIMARY EXAMINER